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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,003	03/22/2001	David M. Sabatini	50347/002004	5682

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/817,003	SABATINI, DAVID M.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *160-177 and 237-246* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *160-177 and 237-246* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 4/24/06 has been acknowledged.
Claims 160-177 and 237-246 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is **571-273-8300.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 160-169, 172-175 and 237-246 are rejected under 35 U.S.C. 102(e) as being anticipated by Hozier (US 5,563,060, 1996), for the same reasons of record as set forth in the office action mailed on 07/12/06.

The scope of instant claims encompasses an array of transfected eukaryotic cells *comprising* a surface having an array of at least 96 locations wherein each location *comprises* eukaryotic cells that are transfected with one or more defined nucleic acid molecules.

Hozier teaches micro libraries for screening cell population. The cited art teaches that micro library comprises microscopic subpopulations immobilized on a surface wherein each subpopulation is formed from between 1 to 1,000,000 cells and the approximate density of said sub-populations is between 10 sub-populations per mm square and $10x10^6$ sub-populations per mm square (col.23, lines 57-67, col.24, lines 60-67). The cited art further teaches that micro library contains cells containing exogenous DNA (col.24, lines 14-18, col.15, lines 24-34). The cited art further teaches micro libraries comprising human genomic or cDNA libraries (col. 25, lines 1-15). The cited art further teaches that micro-libraries comprise variety of cells that include any eukaryotic cell (col. 24, lines

27-35). The cited art further teaches preparation of predetermined arrays (col.11, lines 58-67). In addition the cited art teaches that the cell attachment surfaces include but are not limited to surfaces of polystyrene and treated polystyrene surfaces commonly used in cell culture, plastic and glass surfaces, which may be untreated or treated to aid cell attachment, including those treated with generic preparations e.g., poly-L-lysine, collagen, fibronectin, laminin and the like, or with proprietary preparations like "CELL-TAK" an adhesive protein from a marine mussel, and "MATRIGEL," which aid and promote cell adherence (see col. 9, lines 18-31 col.10 lines 12-33) . Thus the cited art clearly anticipate the invention as claimed.

Response to arguments *(*35 USC § 102: *Hozier)*

The applicant arguments regarding prior issue on pages 8 of response filed on 10/10/06 has been fully considered. The applicant argues that the instant claims has been amended to recite an arrays in which eukaryotic cells are disposed on features comprising one or more defined nucleic acid molecules such that the cells become transfected with the one or more defined nucleic acid molecules when the array is maintained for a suitable period of time, to produce an array of reverse transfected cells. The applicant argues that Hozier teaches arrays in which subpopulations of cells containing exogenous genetic material are immobilized on a surface. The applicant argues that Hozier nowhere teaches or suggests an array comprising a surface in which eukaryotic cells are disposed on features comprising one or more defined nucleic acid molecules in a discrete location, wherein the nucleic acid molecules are so affixed to the surface that the cells become transfected with the one or more defined nucleic acid molecules as recited in claim 160 as amended.

However, applicant's arguments are found not persuasive. Given the broadest reasonable interpretation the instant invention is drawn to an array of transfected eukaryotic cells having an array of at least 96 locations wherein each location *comprises* eukaryotic cells that are transfected with one or more defined nucleic acid molecules. Therefor the invention as claimed reads upon a product by process wherein the final product (*an array of transfected cells attached to any surface*) as claimed

herein is indistinguishable from the product cited in the prior art of record. Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps (see MPEP §2113). Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Thus the cited art clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

Claim 170-171 and 176-177 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hozier (US 5,563,060, 1996) as applied to claims 1160-175 and 237-240 above, and further in view of Montgomery et al (Proc Natl Acad Sci U S A. 95(26): 15502-7, 1998) and Fire et al (US 6506559, 2003).

Hozier is relied upon as described in rejection above. However, Hozier does not teach the use double-stranded RNA molecule or nucleic acid molecule having a modified base or backbone.

Montgomery teaches the double-stranded RNA mediated genetic interference in C.elegans. The cited art teaches a nucleic acid molecule, which encodes double-stranded RNA for RNAi experiments (page 15502, col2. para.2). The cited art teaches gene-specific probes for insitu hybridization, wherein the probe comprises Digoxigenin (DIG)-labeled single stranded DNA probe (page 15503, col.2, para. 3).

Fire et al teaches a method to inhibit expression of a target gene in a cell in vitro comprising introduction of a ribonucleic acid (double-stranded RNA molecule) into the cell in an amount sufficient to inhibit expression of the target gene. The cited art further teaches that the solutions containing duplex RNAs that are capable of inhibiting the different expressed genes can be placed into

individual wells positioned on a micro titer plate as an ordered array, and intact cells/organisms in each well can be assayed for any changes or modifications in behavior or development due to inhibition of target gene activity. The cited art further teaches that the function of the target gene can be assayed from the effects it has on the cell/organism when gene activity is inhibited (see col. 12 lines 46-; col. 26-28).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Taylor in view of Montgomery or Fire by substituting the nucleic acid molecules with a double-stranded RNA molecule, a nucleic acid molecule that interfere with the function of an endogenous gene or a nucleic acid molecule having a modified base or backbone. One would have been motivated to incorporate such a modification to inhibit the expression of a gene of interest. One would have a reasonable expectation of success, since affixing the nucleic acid sequences on various type of tissue culture supports and transfection of cells using the affixed nucleic acid has been routine in the art at the time the instant invention was made. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Response to arguments (*35 USC § 103:* Hozier and Montgomery)

The applicant argues that Hozier and Montgomery do not teach the invention of claim 160, from which claim 176 depend. The applicant argues that the combination of Hozier and Montgomery does not render claim 176 obvious. However, applicant's arguments are found not persuasive for the same reasons of record as set forth above in the prior art rejection as anticipated by Hozier.

Claim Rejections - 35 USC § 102

Claims 160-168, 172-175 and 240-246 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Taylor et al (US 6,103,479, 2000).

The scope of instant claims encompasses an array of transfected eukaryotic cells *comprising* a surface having an array of at least 96 locations wherein each location *comprises* eukaryotic cells that are transfected with one or more defined nucleic acid molecules.

Taylor teaches making of miniaturizes high-throughput cell array and an apparatus for cell-based screening. Regarding claim 160 the cited art teaches spots of eukaryotic cells spotted at the resolution of 200 um or 400 um spot patterns, which is capable of inherently providing spot density of at least 2500 or 625 locations per square centimeter respectively at such a resolution (see figure 3B, col. 7, lines 21-24), which is well with the density of locations claimed in the instant application (i.e. 100-1000 locations per square centimeter. In addition the cited art further discloses miniaturizes high-throughput cell array, which comprises at least 96 locations (see figure 18A-B, col. 8, lines 10-14, col.20, lines 10-15). The cited art teaches that a cell micro array comprises the dimensions of 20mmX30mm (col.16, lines 45-50). The cited art further teaches that each a cell based assay that requires area equivalent to a well size of 0.2 to 1.0mm diameter (col.6, lines 11-19). Accordingly the cited art clearly anticipates an array of at least 100-500 locations having density in the range of 100 locations per square centimeter.

The cited art further teaches that the preferred cell types for the micro-patterned array include lymphocytes, cancer cells, fibroblasts, neurons, fungi, bacteria and other prokaryotic and eukaryotic cells (col.13 lines 5-35). The cited art further teaches micro-patterns at discrete locations comprises array of different forms, which accommodate a sample size from 1 nanoliter (nl) to 1000nl (col.9 lines 7-10). The cited art further teaches that the size of a well on micro-patterned array ranges from 200 μm to 400μm, which would inherently provides providing spot density of at least 2500 or 625 locations per square centimeter (see figure 3B, col. 7, lines 21-24). Regarding claims 161-164 and 166 the cited art teaches that the cells attaches to the wells can be modified with luminescent of cell chemical or molecular properties. The indicators can be introduced into the

cells before or after the cells were seeded onto array by any one or combination of variety of physical methods such as diffusion across the cell membrane, mechanical perturbation of cell membrane or genetic engineering so that they express under prescribed conditions. The cited art further teaches the use of reporter genes which encodes chemiluminescent proteins, which permits the analysis of the physiological state of cells when contacted with drugs or other reactive substances (Col.12 lines 44-67, col. 13, line 1-4, col.13, lines 29-30). Regarding claim 165 the cited art teaches that the cells suspended in culture media at concentration from about 10^3-10^7 cells per ml are incubated in contact with the wells. The cited art teaches that the density of cells attached to wells is controlled by the cell density in the cell suspension, time permitted for cell attachment to the well surface (col.12, lines 13-36). Thus given the broadest reasonable interpretation the cited art clearly teaches an array of transfected eukaryotic cells as claimed.

Response to arguments (35 USC § 102: *Taylor)*

Applicant's arguments filed on page 10 dated 10/10/06 regarding prior art issues have been fully considered. The applicant argues that eventhough Taylor teaches arrays of genetically engineered cells (e.g., a reporter or a cell surface marker), the cited art nowhere teaches or suggests a surface having at least 96 locations, wherein each location comprises eukaryotic cells disposed on a feature comprising one or more defined nucleic acid molecules in a discrete location as recited in claim 160.

However, applicant's arguments are found not persuasive for the same reasons of record as set forth above because the cited art clearly teaches:

i) spots of eukaryotic cells spotted at the resolution of 200 um or 400 um spot patterns, which is capable of inherently providing spot density of at least 2500 or 625 locations per square centimeter respectively which is well within the range of "at least 96 locations" as claimed in the instant invention (see figure 3B, col. 7, lines 21-24), which is well with the density of locations claimed in the instant application (i.e. 100-1000 locations per square centimeter.

ii) miniaturizes high-throughput cell array, which comprises at least 96 locations (**see figure 18A-B,** col. 8, lines 10-14, col.20, lines 10-15) and a cell micro array comprises the dimensions of 20mmX30mm (col.16, lines 45-50).

iii) a cell based assay that requires area equivalent to a well size of 0.2 to 1.0mm diameter (col.6, lines 11-19), which at this resolution is capable of providing at least 100-500 locations having density well within the range of 100 locations per square centimeter as claimed in the instant application.

Furthermore product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps (see MPEP §2113). Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Thus given the broadest reasonable interpretation the invention as claimed obvious over the cited art of record if not anticipated.

Claim Rejections - 35 USC § 103

Claim 170-171 and 176-177 is rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al (US 6103,479 2000) as applied to claims 160-168, 171-174 and 240 above, and further in view of Montgomery et al (Proc Natl Acad Sci U S A. 95(26): 15502-7, 1998) and Fire et al (US 6506559, 2003).

Taylor et al is relied upon as described in rejection above. However, Taylor does not teach the use double-stranded RNA molecule or nucleic acid molecule having a modified base or backbone.

Montgomery teaches the double-stranded RNA mediated genetic interference in C.elegans. The cited art teaches a nucleic acid molecule, which encodes double-stranded RNA for RNAi experiments (page 15502, col2. para.2).

The cited art teaches gene-specific probes for insitu hybridization, wherein the probe comprises Digoxigenin (DIG)-labeled single stranded DNA probe (page 15503, col.2, para. 3).

Fire et al teaches a method to inhibit expression of a target gene in a cell in vitro comprising introduction of a ribonucleic acid (double-stranded RNA molecule) into the cell in an amount sufficient to inhibit expression of the target gene. The cited art further teaches that the solutions containing duplex RNAs that are capable of inhibiting the different expressed genes can be placed into individual wells positioned on a micro titer plate as an ordered array, and intact cells/organisms in each well can be assayed for any changes or modifications in behavior or development due to inhibition of target gene activity. The cited art further teaches that the function of the target gene can be assayed from the effects it has on the cell/organism when gene activity is inhibited (see col. 12 lines 46-; col. 26-28).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the invention of Taylor in view of Montgomery and Fire by substituting the nucleic acid molecules with a double-stranded RNA molecule, a nucleic acid molecule that interfere with the function of an endogenous gene or a nucleic acid molecule having a modified base or backbone. One would have been motivated to incorporate such a modification to inhibit the expression of a gene of interest. One would have a reasonable expectation of success, since affixing the nucleic acid sequences on various type of tissue culture supports and transfection of cells using the affixed nucleic acid has been routine in the art at the time the instant invention was made. Thus the invention as claimed is *prima facie* obvious in view of cited prior art of record.

Response to Arguments *(Taylor and Montgomery)*

The applicant fails to provide any remarks that would have addressed Taylor in view of Montgomery

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**

SUMESH KAUSHAL
PRIMARY EXAMINER
ART UNIT 1633